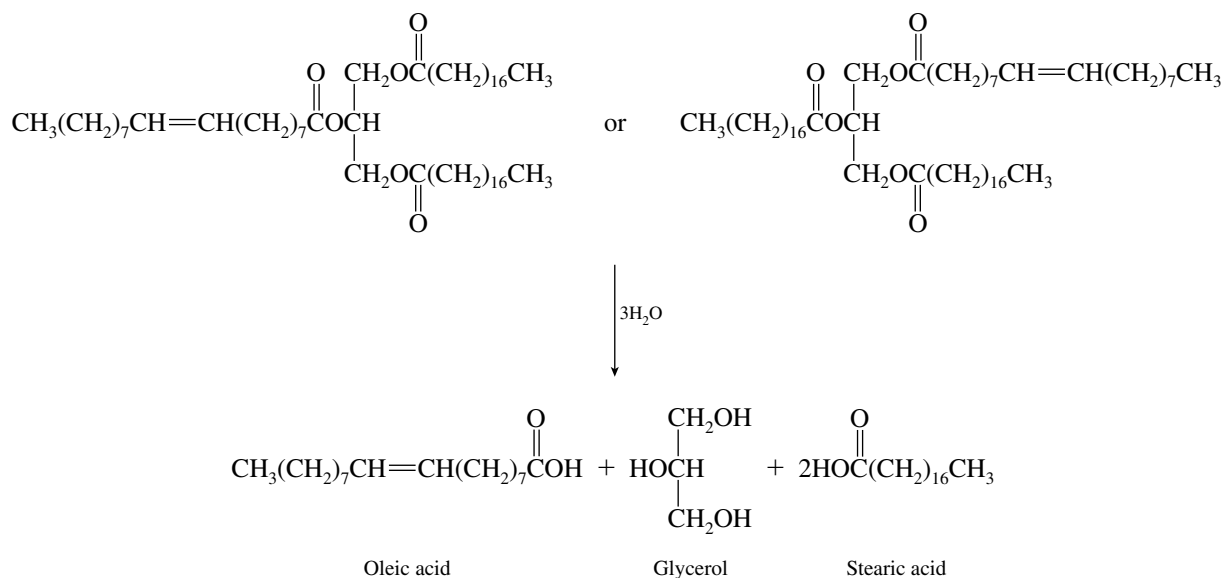


## CHAPTER 26

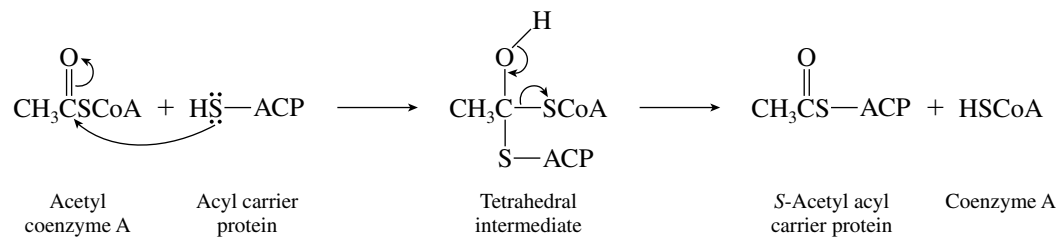
### LIPIDS

#### SOLUTIONS TO TEXT PROBLEMS

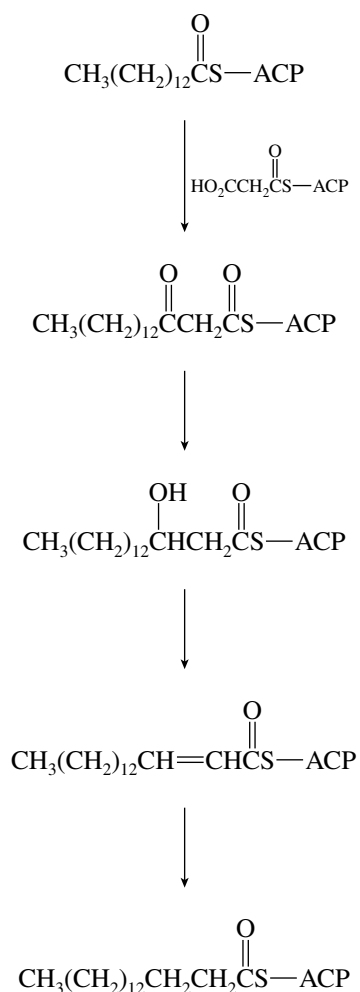
- 26.1** The triacylglycerol shown in text Figure 26.2a, with an oleyl group at C-2 of the glycerol unit and two stearyl groups at C-1 and C-3, yields stearic and oleic acids in a 2 : 1 molar ratio on hydrolysis. A constitutionally isomeric structure in which the oleyl group is attached to C-1 of glycerol would yield the same hydrolysis products.



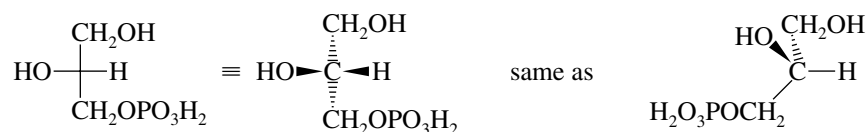
- 26.2 The sulfur of acyl carrier protein acts as a nucleophile and attacks the acetyl group of acetyl coenzyme A.



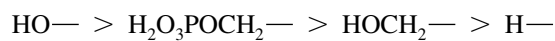
- 26.3 Conversion of acyl carrier protein-bound tetradecanoate to hexadecanoate proceeds through the series of intermediates shown.



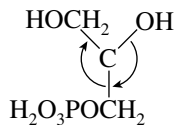
- 26.4 The structure of L-glycerol 3-phosphate is shown in a Fischer projection. Translate the Fischer projection to a three-dimensional representation.



The order of decreasing sequence rule precedence is



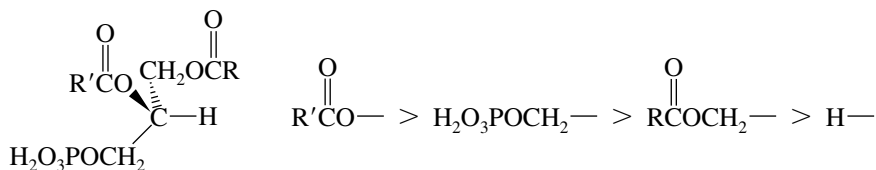
When the three-dimensional formula is viewed from a perspective in which the lowest ranked substituent is away from us, we see



Order of decreasing rank is clockwise, therefore *R*.

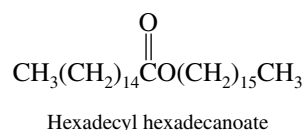
The absolute configuration is *R*.

The conversion of *L*-glycerol 3-phosphate to a phosphatidic acid does not affect any of the bonds to the stereogenic center, nor does it alter the sequence rule ranking of the substituents.

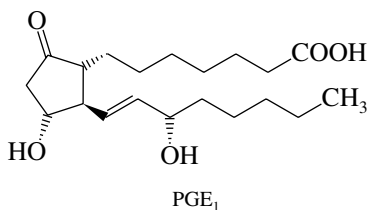


The absolute configuration is *R*.

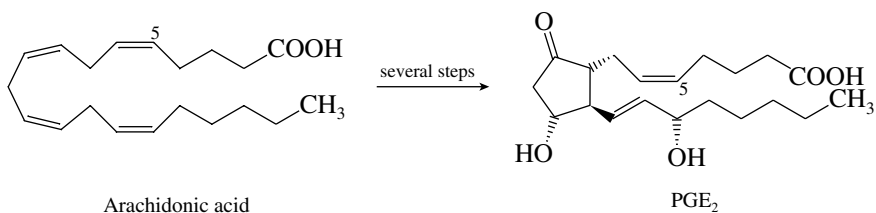
- 26.5** Cetyl palmitate (hexadecyl hexadecanoate) is an ester in which both the acyl group and the alkyl group contain 16 carbon atoms.




- 26.6** The structure of PGE<sub>1</sub> is found in text Figure 26.5.

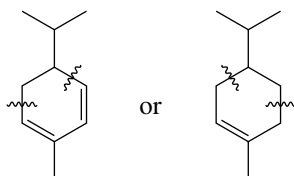


The problem states that PGE<sub>2</sub> has one more double bond than PGE<sub>1</sub> and that it is biosynthesized from arachidonic acid. Arachidonic acid (text Table 26.1) has a double bond at C-5, and thus PGE<sub>2</sub> has the structure shown.

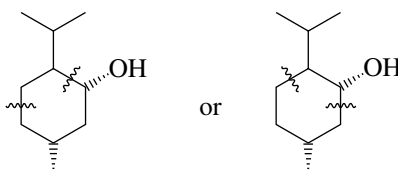


- 26.7 Isoprene units are  fragments in the carbon skeleton. Functional groups and multiple bonds are ignored when structures are examined for the presence of isoprene units.

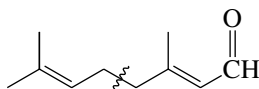
**$\alpha$ -Phellandrene** (two equally correct answers):



**Menthol** (same carbon skeleton as  $\alpha$ -phellandrene but different functionality):

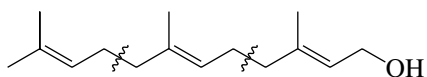


**Citral:**

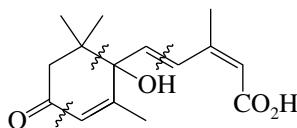


**$\alpha$ -Selinene** is shown in text Section 26.7.

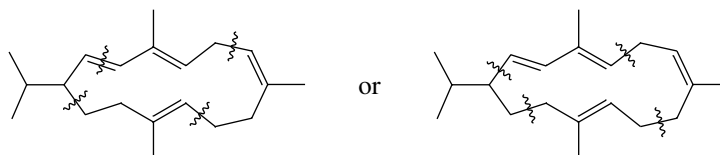
**Farnesol:**



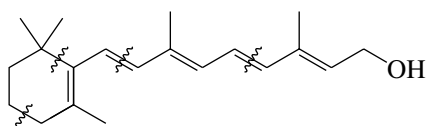
**Abscisic acid:**



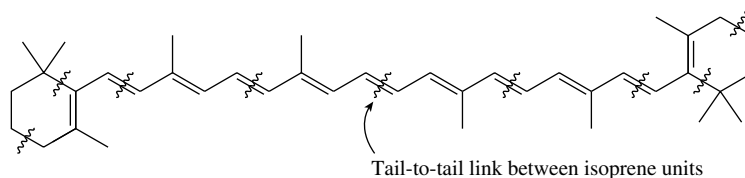
**Cembrene** (two equally correct answers):



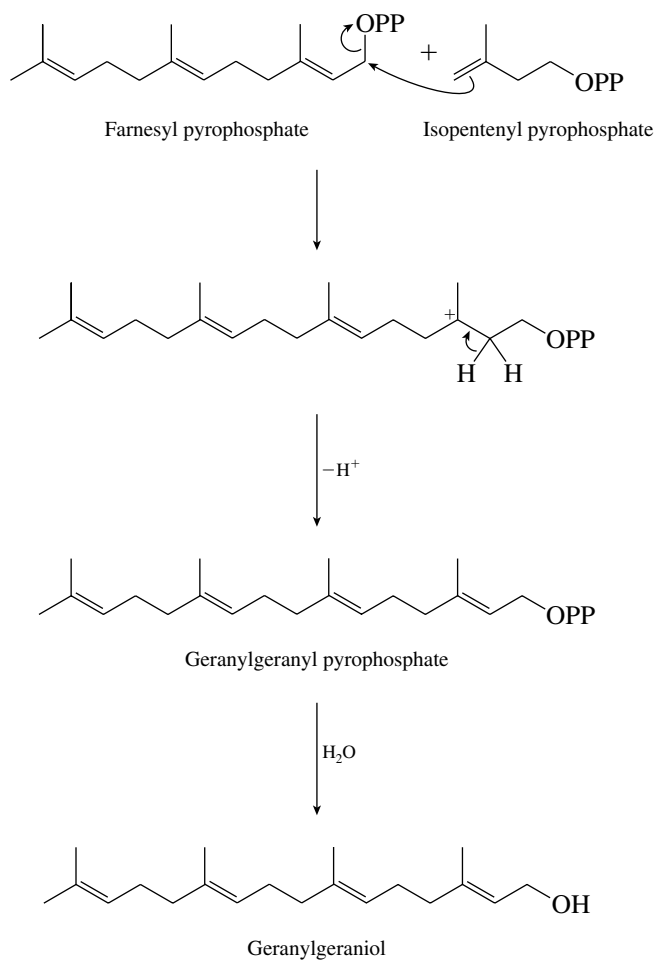
**Vitamin A:**



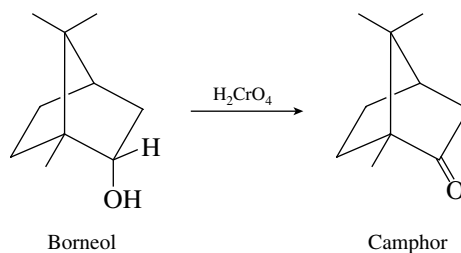
- 26.8  $\beta$ -Carotene is a tetraterpene because it has 40 carbon atoms. The tail-to-tail linkage is at the midpoint of the molecule and connects two 20-carbon fragments.



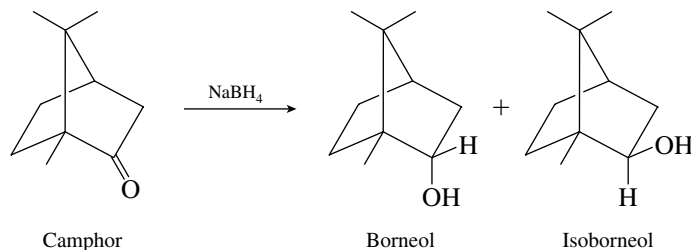
- 26.9 Isopentenyl pyrophosphate acts as an alkylating agent toward farnesyl pyrophosphate. Alkylation is followed by loss of a proton from the carbocation intermediate, giving geranylgeranyl pyrophosphate. Hydrolysis of the pyrophosphate yields geranylgeraniol.



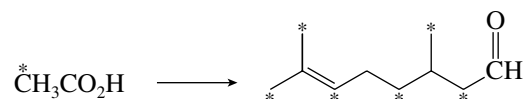
- 26.10 Borneol, the structure of which is given in text Figure 26.7, is a secondary alcohol. Oxidation of borneol converts it to the ketone camphor.



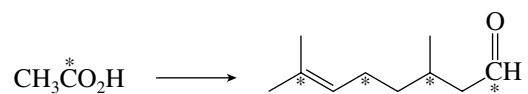
Reduction of camphor with sodium borohydride gives a mixture of stereoisomeric alcohols, of which one is borneol and the other isborneol.



- 26.11** Figure 26.8 in the text describes the distribution of  $^{14}\text{C}$  (denoted by \*) in citronellal biosynthesized from acetate enriched with  $^{14}\text{C}$  in its methyl group.

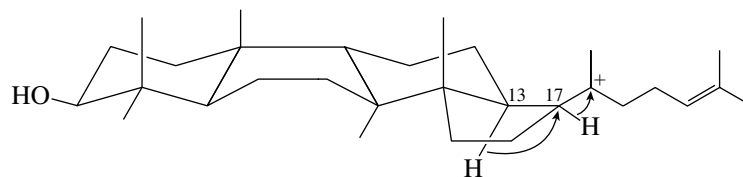


If, instead, acetate enriched with  $^{14}\text{C}$  at its carbonyl carbon were used, exactly the opposite distribution of the  $^{14}\text{C}$  label would be observed.



When  $^{14}\text{CH}_3\text{CO}_2\text{H}$  is used, C-2, C-4, C-6, C-8, and both methyl groups of citronellal are labeled. When  $\text{CH}_3^{14}\text{CO}_2\text{H}$  is used, C-1, C-3, C-5, and C-7 are labeled.

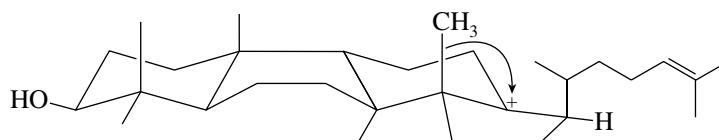
- 26.12** (b) The hydrogens that migrate in step 3 are those at C-13 and C-17 (steroid numbering).



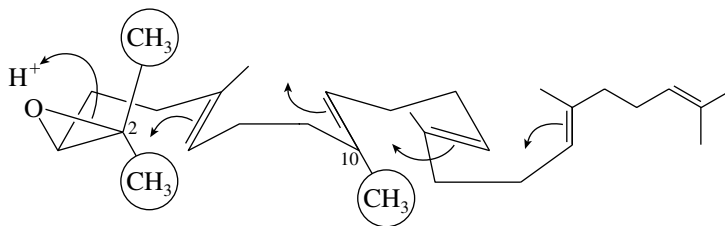
As shown in the coiled form of squalene 2,3-epoxide, these correspond to hydrogens at C-14 and C-18 (systematic IUPAC numbering).



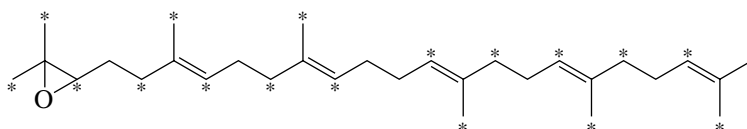
- (c) The carbon atoms that form the C, D ring junction in cholesterol are C-14 and C-15 of squalene 2,3-epoxide. It is the methyl group at C-15 of squalene 2,3-epoxide that becomes the methyl group at this junction in cholesterol.



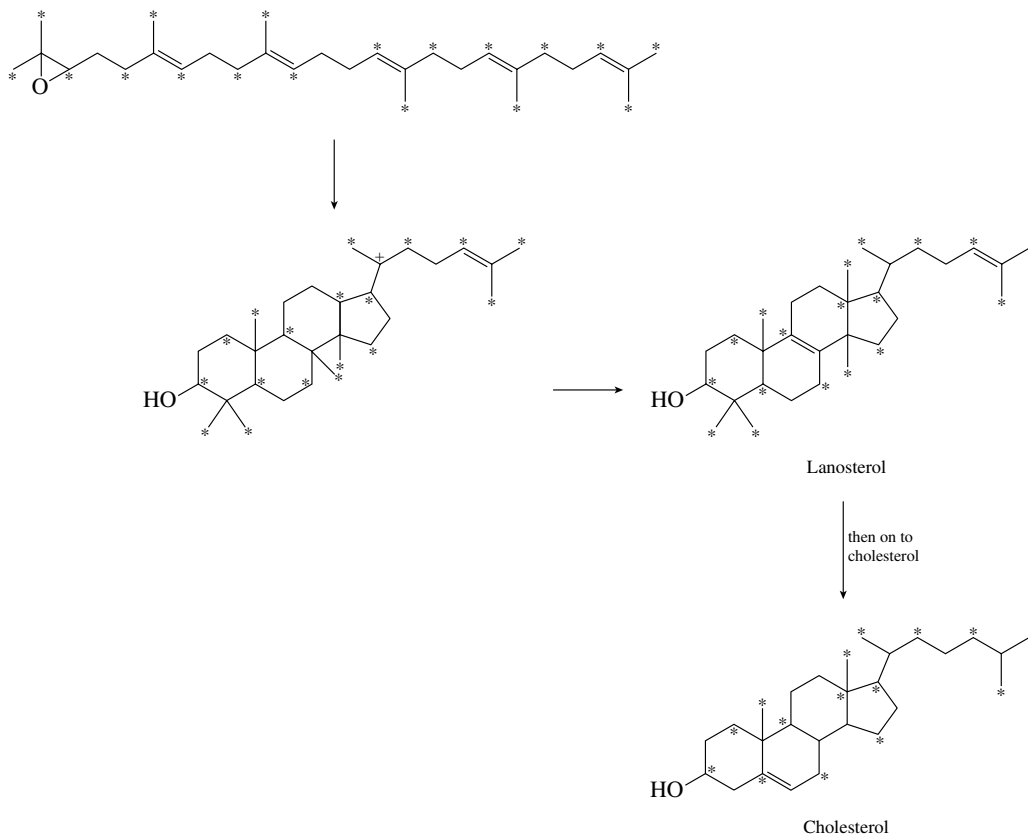
- (d) The methyl groups that are lost are the methyl substituents at C-2 and C-10 plus the methyl group that is C-1 of squalene 2,3-epoxide.



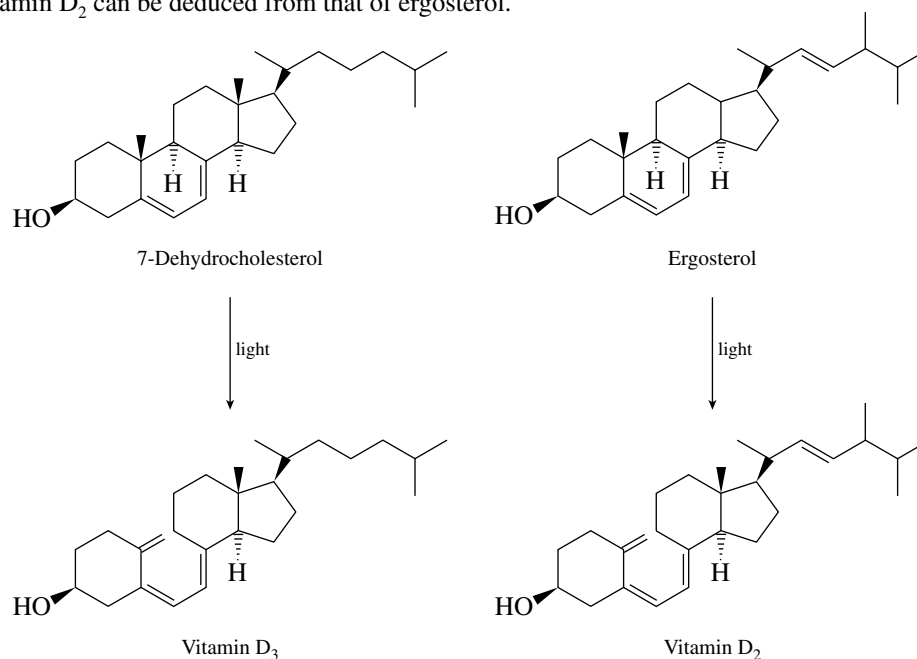
- 26.13** Tracking the  $^{14}\text{C}$  label of  $^{14}\text{CH}_3\text{CO}_2\text{H}$  through the complete biosynthesis of cholesterol requires a systematic approach. First, by analogy with Problem 26.11, we can determine the distribution of  $^{14}\text{C}$  (denoted by \*) in squalene 2,3-epoxide.



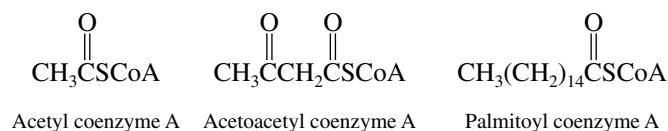
Next, follow the path of the  $^{14}\text{C}$ -enriched carbons in the cyclization of squalene 2,3-epoxide to lanosterol.



- 26.14 By analogy to the reaction in which 7-dehydrocholesterol is converted to vitamin D<sub>3</sub>, the structure of vitamin D<sub>2</sub> can be deduced from that of ergosterol.



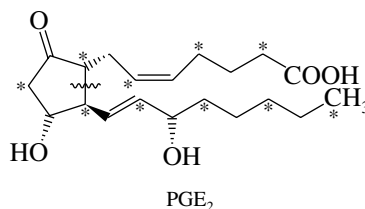
- 26.15 (a) Fatty acid biosynthesis proceeds by the joining of acetate units.



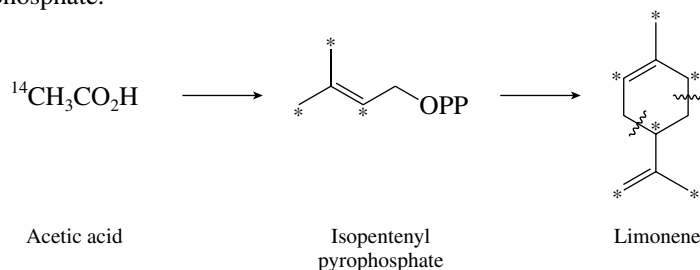
Thus, the even-numbered carbons will be labeled with <sup>14</sup>C when palmitic acid is biosynthesized from <sup>14</sup>CH<sub>3</sub>CO<sub>2</sub>H.



- (b) As noted in Problem 26.6, arachidonic acid (Table 26.1) is the biosynthetic precursor of PGE<sub>2</sub>. The distribution of the <sup>14</sup>C label in PGE<sub>2</sub> biosynthesized from <sup>14</sup>CH<sub>3</sub>CO<sub>2</sub>H reflects the fatty acid origin of the prostaglandins.

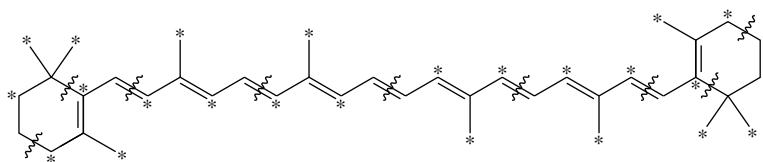


- (c) Limonene is a monoterpene, biosynthesized from acetate by way of mevalonate and isopentenyl pyrophosphate.

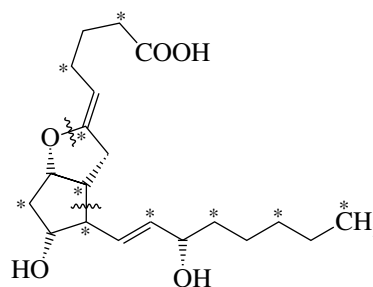




- (d) The distribution of the  $^{14}\text{C}$  label in  $\beta$ -carotene becomes evident once its isoprene units are identified.

 $\beta$ -Carotene

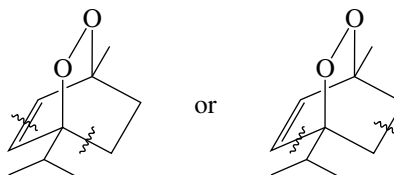
- 26.16** The carbon chain of prostacyclin is derived from acetate by way of a  $\text{C}_{20}$  fatty acid. Trace a continuous chain of 20 carbons beginning with the carboxyl group. Even-numbered carbons are labeled with  $^{14}\text{C}$  when prostacyclin is biosynthesized from  $^{14}\text{CH}_3\text{CO}_2\text{H}$ .



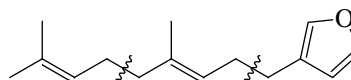
Prostacyclin

- 26.17** The isoprene units in the designated compounds are shown by disconnections in the structural formulas.

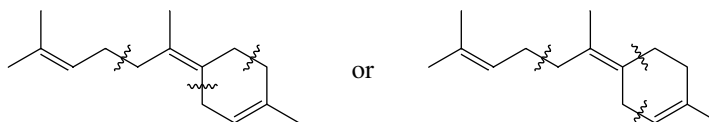
- (a) Ascaridole:



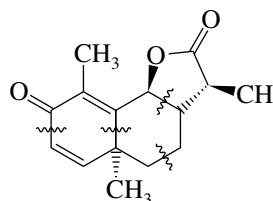
- (b) Dendrolasin:



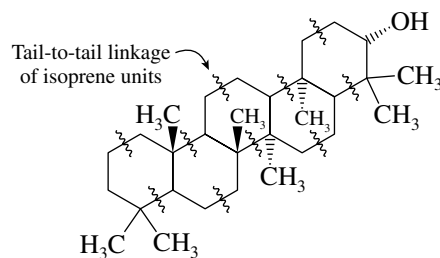
- (c)  $\gamma$ -Bisabolene



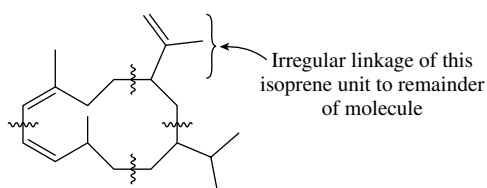
- (d)  $\alpha$ -Santonin



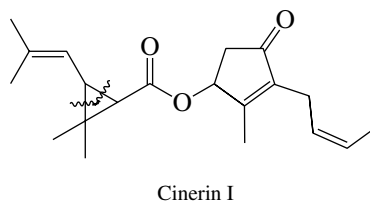
(e) Tetrahymanol



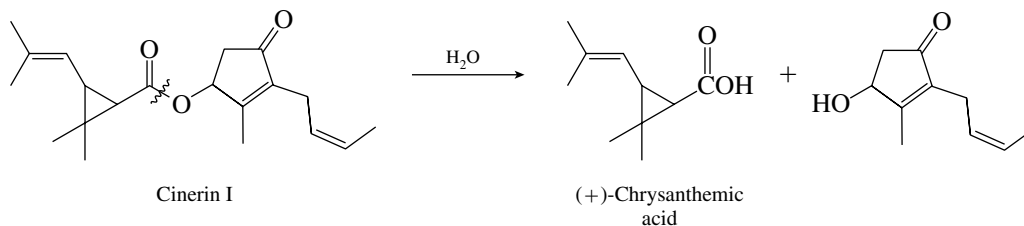
**26.18** Of the four isoprene units of cubitene, three of them are joined in the usual head-to-tail fashion, but the fourth one is joined in an irregular way.



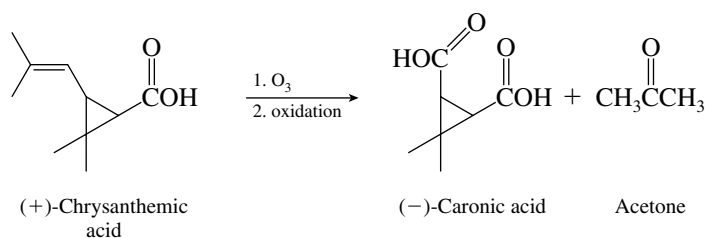
**26.19** (a) Cinerin I is an ester, the acyl portion of which is composed of two isoprene units, as follows:



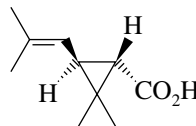
(b) Hydrolysis of cinerin I involves cleavage of the ester unit.



Chrysanthemic acid has the constitution shown in the equation. Its stereochemistry is revealed by subsequent experiments.

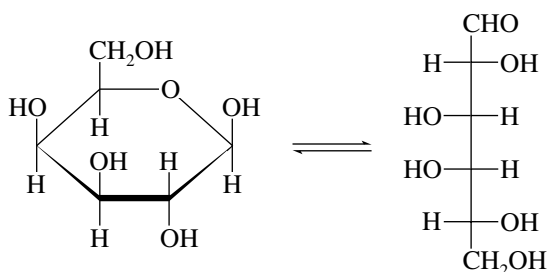


Because caronic acid is optically active, its carboxyl groups must be trans to each other. (The cis stereoisomer is an optically inactive meso form.) The structure of (+)-chrysanthemic acid must therefore be either the following or its mirror image.



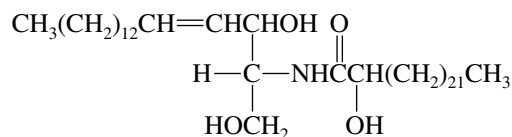
The carboxyl group and the 2-methyl-1-propenyl side chain must be trans to each other.

- 26.20 (a) Hydrolysis of phrenosine cleaves the glycosidic bond. The carbohydrate liberated by this hydrolysis is D-galactose.

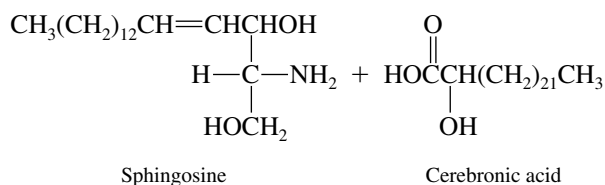


Phrenosine is a  $\beta$ -glycoside of D-galactose.

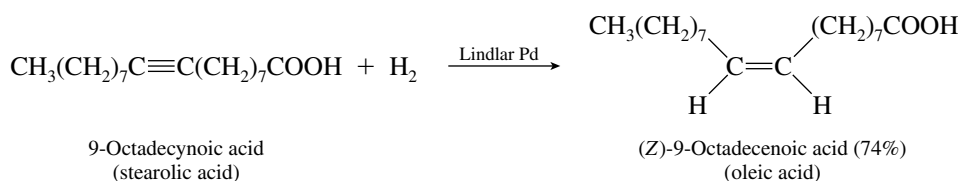
- (b) The species that remains on cleavage of the galactose unit has the structure



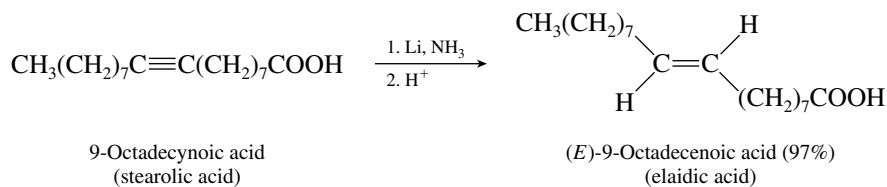
The two substances, sphingosine and cerebronic acid, that are formed along with D-galactose arise by hydrolysis of the amide bond.



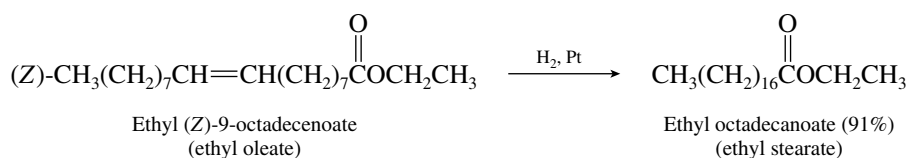
- 26.21 (a) Catalytic hydrogenation over Lindlar palladium converts alkynes to cis alkenes.



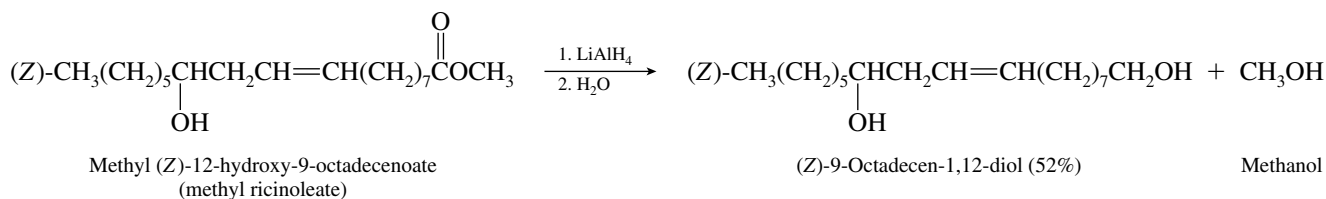
- (b) Carbon–carbon triple bonds are converted to trans alkenes by reduction with lithium and ammonia.



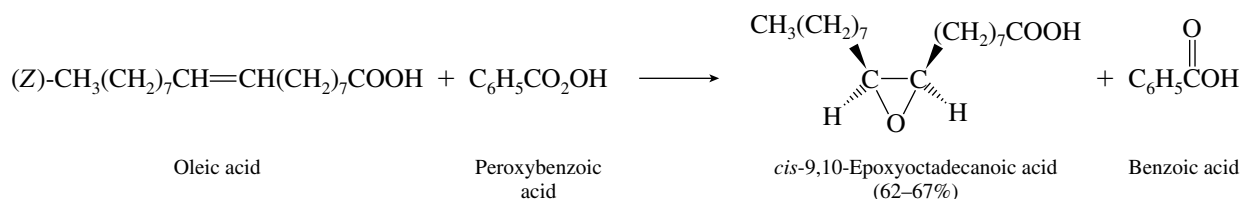
- (c) The carbon–carbon double bond is hydrogenated readily over a platinum catalyst. Reduction of the ester function does not occur.



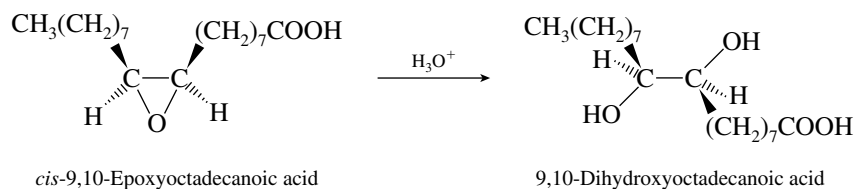
- (d) Lithium aluminum hydride reduces the ester function but leaves the carbon–carbon double bond intact.



- (e) Epoxidation of the double bond occurs when an alkene is treated with a peroxy acid. The reaction is stereospecific; substituents that are cis to each other in the alkene remain cis in the epoxide.

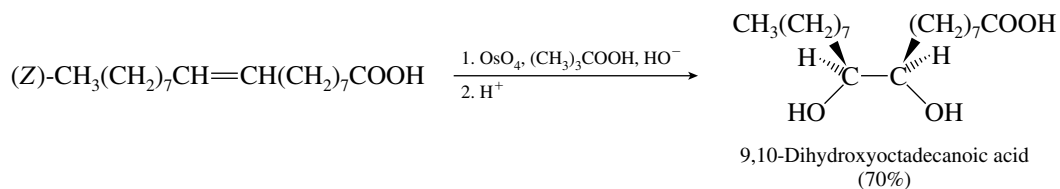


- (f) Acid-catalyzed hydrolysis of the epoxide yields a diol; its stereochemistry corresponds to net anti hydroxylation of the double bond of the original alkene.



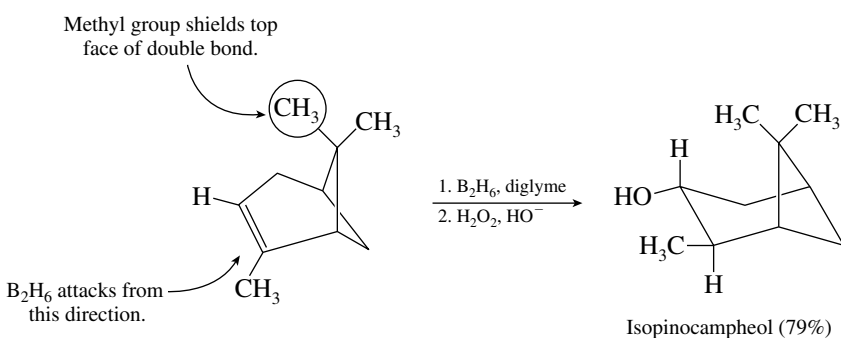
The product is chiral but is formed as a racemic mixture containing equal amounts of the 9*R*,10*R* and 9*S*,10*S* stereoisomers when the starting epoxide is racemic.

- (g) Hydroxylation of carbon–carbon double bonds with osmium tetroxide proceeds with syn addition of hydroxyl groups.

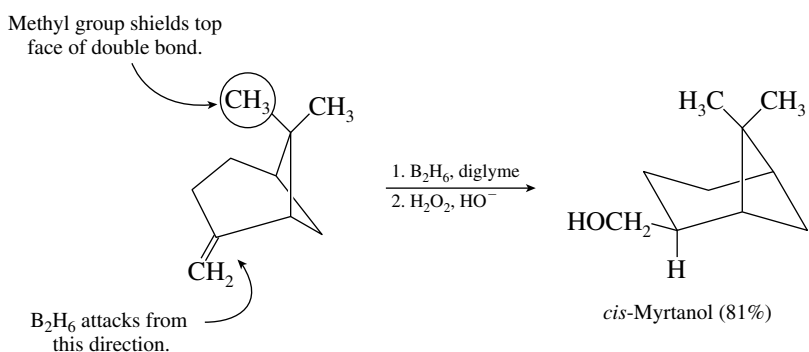


The product is chiral but is formed as a racemic mixture containing equal amounts of the 9*R*,10*S* and 9*S*,10*R* stereoisomers.

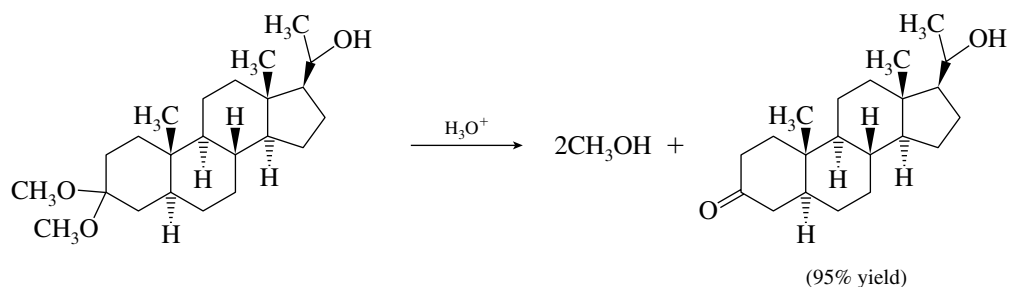
- (h) Hydroboration–oxidation gives syn hydration of carbon–carbon double bonds with a regioselectivity contrary to Markovnikov’s rule. The reagent attacks the less hindered face of the double bond of  $\alpha$ -pinene.



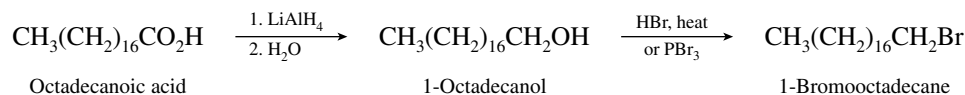
- (i) The starting alkene in this case is  $\beta$ -pinene. As in the preceding exercise with  $\alpha$ -pinene, diborane adds to the bottom face of the double bond.



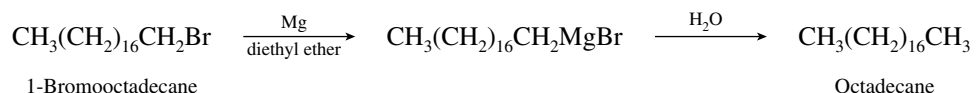
- (j) The starting material is an acetal. It undergoes hydrolysis in dilute aqueous acid to give a ketone.



- 26.22 (a) There are no direct methods for the reduction of a carboxylic acid to an alkane. A number of indirect methods that may be used, however, involve first converting the carboxylic acid to an alkyl bromide via the corresponding alcohol.

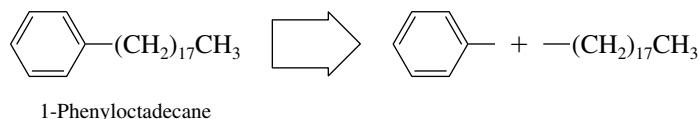


Once the alkyl bromide is in hand, it may be converted to an alkane by conversion to a Grignard reagent followed by addition of water.

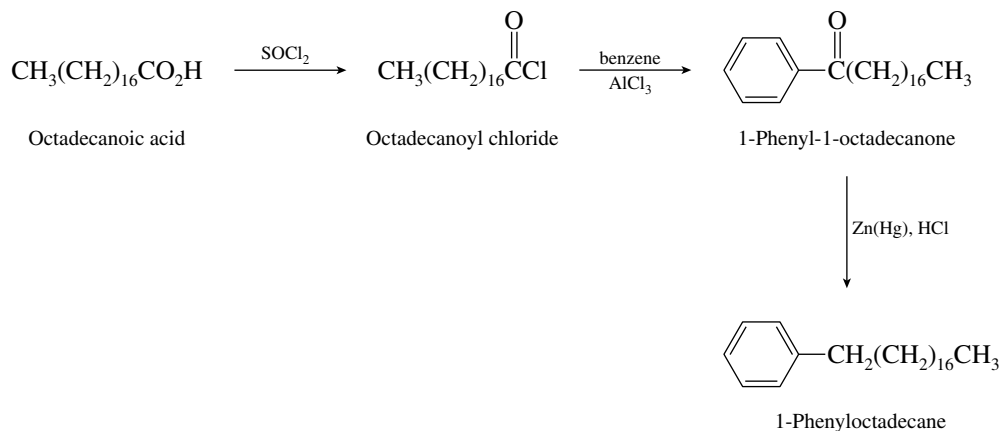


Other routes are also possible. For example, E2 elimination from 1-bromooctadecane followed by hydrogenation of the resulting alkene will also yield octadecane.

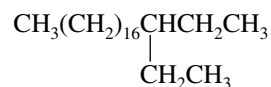
- (b) Retrosynthetic analysis reveals that the 18-carbon chain of the starting material must be attached to a benzene ring.



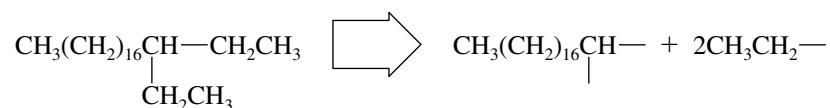
The desired sequence may be carried out by a Friedel–Crafts acylation, followed by Clemmensen or Wolff–Kishner reduction of the ketone.



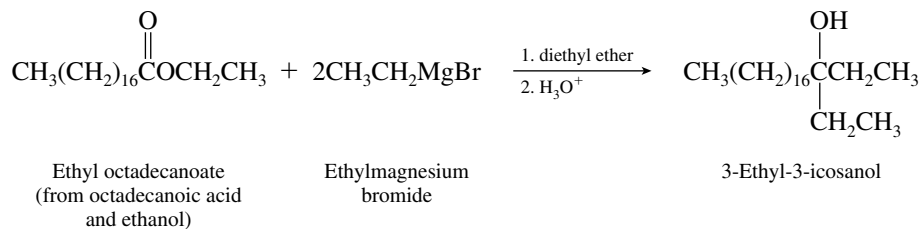
- (c) First examine the structure of the target molecule 3-ethylicosane.



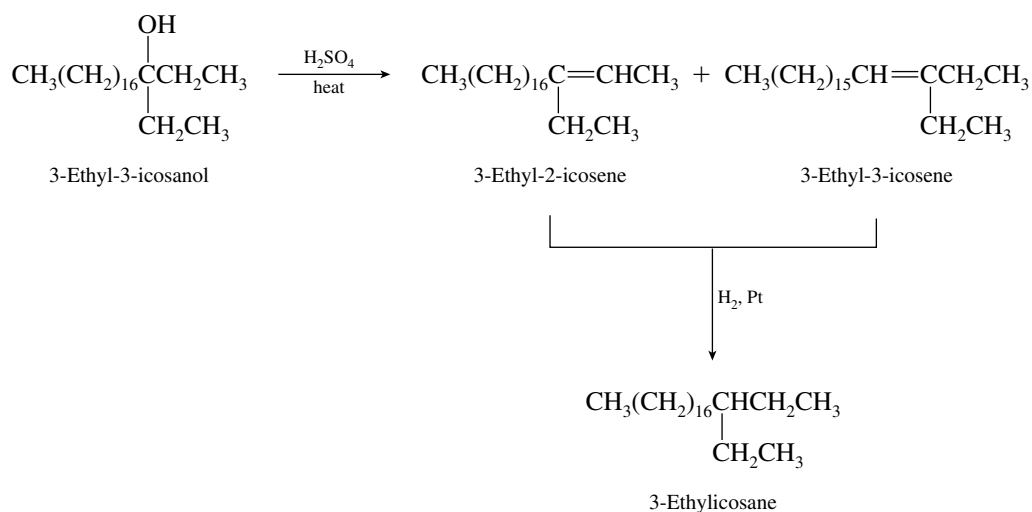
Retrosynthetic analysis reveals that two ethyl groups have been attached to a C<sub>18</sub> unit.



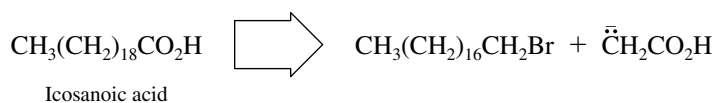
The necessary carbon-carbon bonds can be assembled by the reaction of an ester with two moles of a Grignard reagent.



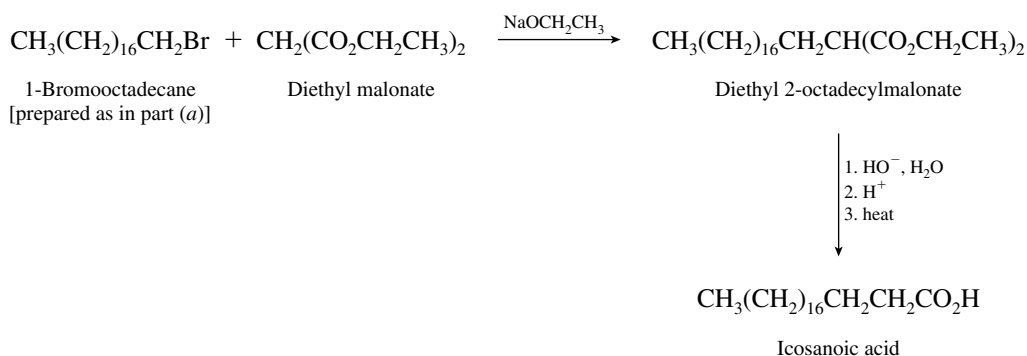
With the correct carbon skeleton in place, all that is needed is to convert the alcohol to the alkene. This can be accomplished by dehydration and reduction.



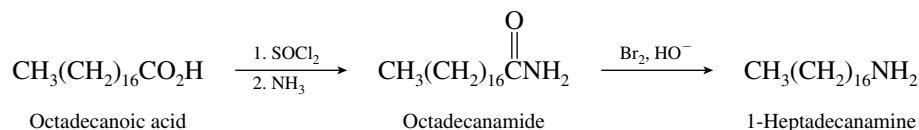
(d) Icosanoic acid contains two more carbon atoms than octadecanoic acid.



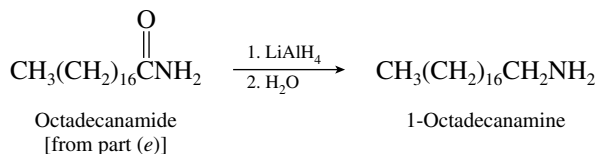
A reasonable approach utilizes a malonic ester synthesis.



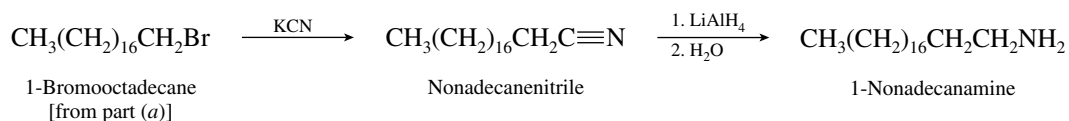
- (e) The carbon chain must be shortened by one carbon atom in this problem. A Hofmann rearrangement (text Section 20.17) is indicated.



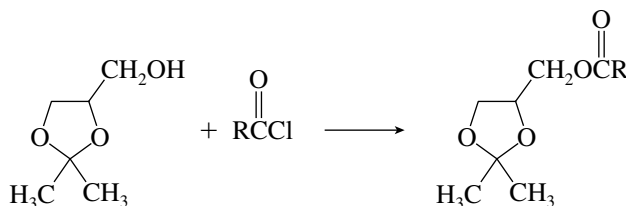
- (f) Lithium aluminum hydride reduction of octadecanamide gives the corresponding amine.



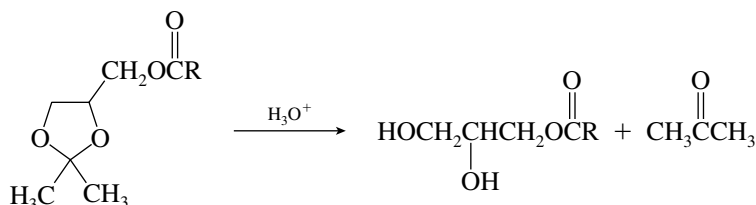
- (g) Chain extension can be achieved via cyanide displacement of bromine from 1-bromooctadecane. Reduction of the cyano group completes the synthesis.



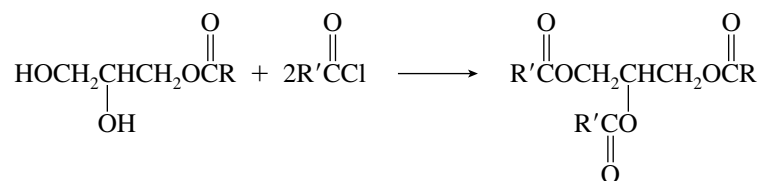
**26.23** First acylate the free hydroxyl group with an acyl chloride.



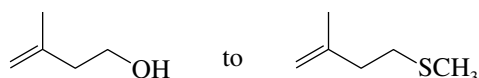
Treatment with aqueous acid brings about hydrolysis of the acetal function.



The two hydroxyl groups of the resulting diol are then esterified with 2 moles of the second acyl chloride.

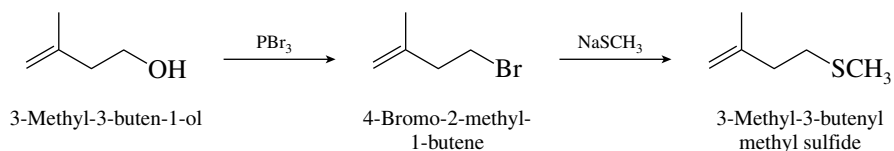


**26.24** The overall transformation



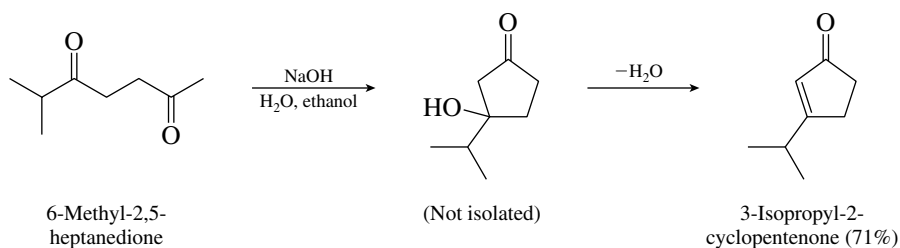


requires converting the alcohol function to some suitable leaving group, followed by substitution by an appropriate nucleophile.

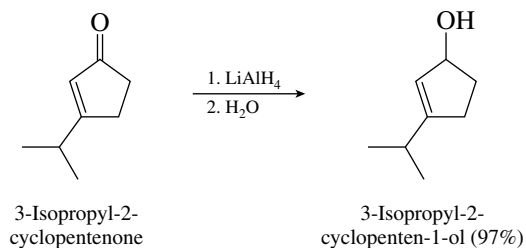


As reported in the literature, the alcohol was converted to its corresponding *p*-toluenesulfonate ester and this substance was then used as the substrate in the nucleophilic substitution step to produce the desired sulfide in 76% yield.

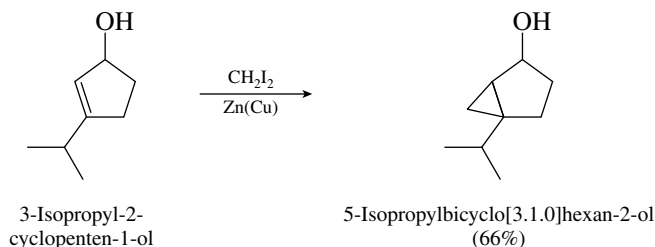
**26.25** The first transformation is an intramolecular aldol condensation. This reaction was carried out under conditions of base catalysis.



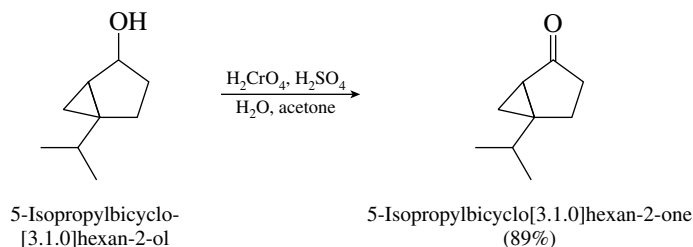
The next step is reduction of a ketone to a secondary alcohol. Lithium aluminum hydride is suitable; it reduces carbonyl groups but leaves the double bond intact.



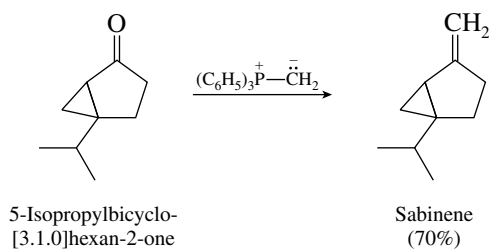
Conversion of an alkene to a cyclopropane can be accomplished to using the Simmons–Smith reagent (iodomethylzinc iodide).



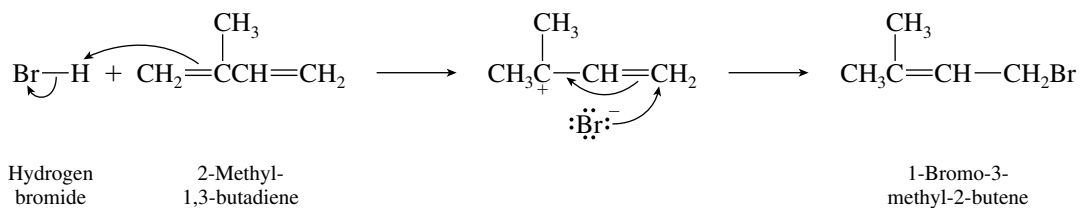
Oxidation of the secondary alcohol to the ketone can be accomplished with any of a number of oxidizing agents. The chemists who reported this synthesis used chromic acid.



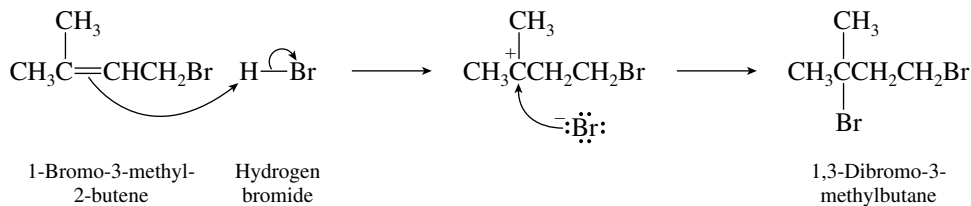
A Wittig reaction converts the ketone to sabinene.



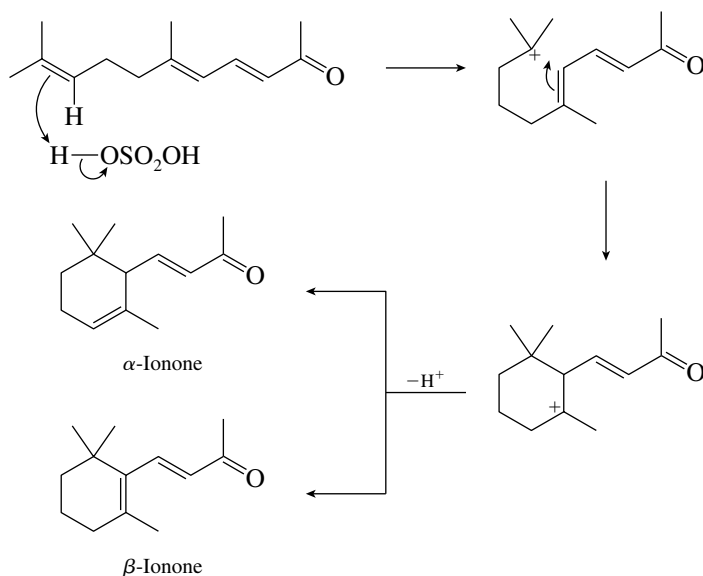
26.26 The first step is a 1,4 addition of hydrogen bromide to the conjugated diene system of isoprene.



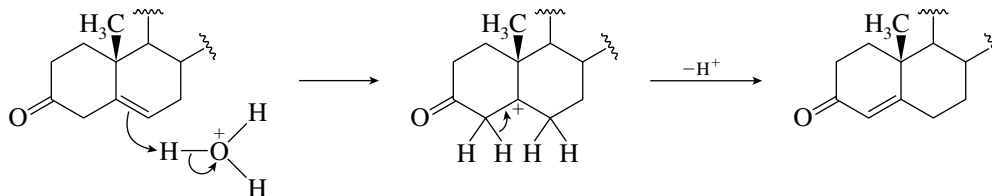
This is followed by Markovnikov addition of hydrogen bromide to the remaining double bond.



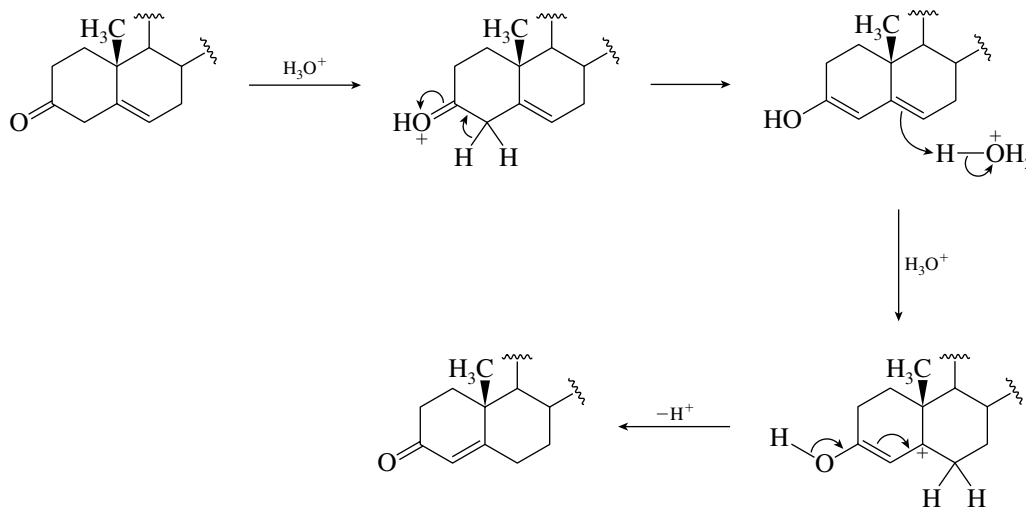
26.27 A reasonable mechanism is protonation of the isolated carbon-carbon double bond, followed by cyclization.



- 26.28 The double bond has a tendency to become conjugated with the carbonyl group. Two mechanisms are more likely than any others under conditions of acid catalysis. One of these involves protonation of the double bond followed by loss of a proton from C-4.



The other mechanism proceeds by enolization followed by proton-induced double-bond migration.

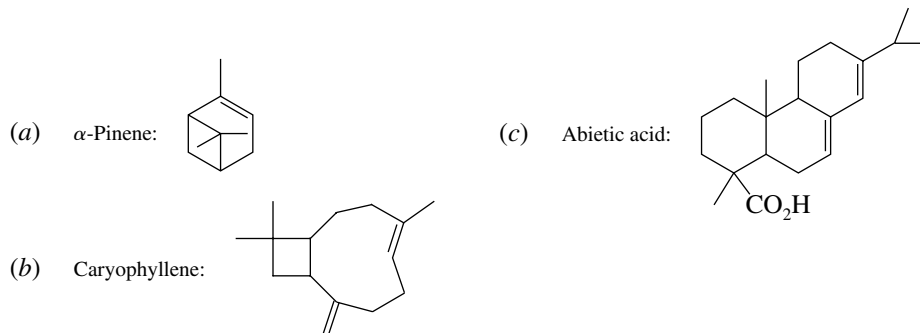


- 26.29 See the June, 1995, issue of the *Journal of Chemical Education*, pages 541–542, for the solution to this problem.
- 26.30 Solutions to molecular modeling exercises are not provided in this *Study Guide and Solutions Manual*. You should use *Learning By Modeling* for this exercise.

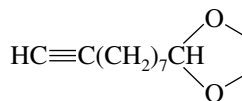
## SELF-TEST

### PART A

- A-1. Write a balanced chemical equation for the basic hydrolysis of tristearin.
- A-2. Both waxes and fats are lipids that contain the ester functional group. In what way do the structures of these lipids differ?
- A-3. Classify each of the following isoprenoid compounds as a monoterpene, a diterpene, and so on. Indicate with dashed lines the isoprene units that make up each structure.

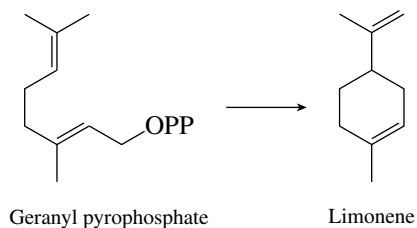


- A-4. Propose a series of synthetic steps to carry out the preparation of oleic acid [(Z)-9-octadecenoic acid] from compound A. You may use any necessary organic or inorganic reagents.



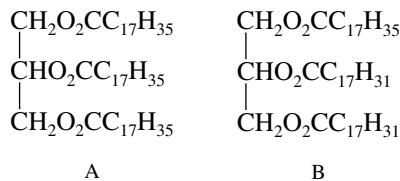
A

- A-5. Write a mechanism for the biosynthetic pathway by which limonene is formed from geranyl pyrophosphate.

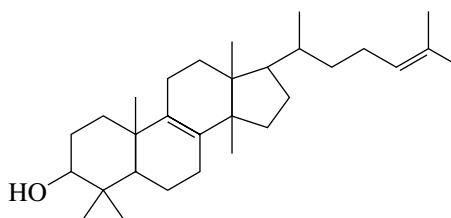


## PART B

- B-1. A major component of a lipid bilayer is
- A triacylglycerol such as tristearin
  - Phosphatidylcholine, also known as lecithin
  - A sterol such as cholesterol
  - A prostaglandin such as PGE<sub>1</sub>
- B-2. Compare the following two triacylglycerols:



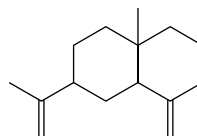
- The melting point of A will be higher.
  - The melting point of B will be higher.
  - The melting points of A and B will be the same.
  - No comparison of melting points can be made.
- B-3. Lanosterol, a biosynthetic precursor of cholesterol, exists naturally as a single enantiomer. How many *possible* stereoisomers having the lanosterol skeleton are there?



Lanosterol

- (a) 7                      (b) 64                      (c) 128                      (d) 256

**B-4.** The compound whose carbon skeleton is shown, known as selinene, is found in celery.



This substance is an example of a

- (a) Monoterpene (c) Sesquiterpene  
 (b) Diterpene (d) Triterpene

**B-5.** Which of the following correctly represents the isoprenoid units of selinene?

- (a) (c) Both of these are acceptable
- (b) (d) Neither of these is acceptable

**B-6.** What is the distribution of radioactive carbon ( $^{14}\text{C}$ ) in isopentenyl pyrophosphate biosynthesized from acetic acid labelled with  $^{14}\text{C}$  at its carboxyl carbon ( $\text{CH}_3^*\text{CO}_2\text{H}$ )?  $^{14}\text{C}$  is indicated by an asterisk (\*) in the structures.

- (a) (d) (b) (e) (c)